New Claim 4 has been added to more clearly claim aspects of the invention. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least at page 12, line 32 - page 13, line 2.

New claim 5 has been added to more clearly claim aspects of the invention. Claim 9 finds support throughout the specification as originally filed, with particular support being found at least at page 13, lines 2-8.

As the amendment of Claim 2 and new claims 4 and 5 are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry therefore is respectfully requested.

III. Rejection of Claims Under 35 U.S.C. § 101

The Action continues to reject the pending claims under 35 U.S.C. § 101, allegedly because the claimed invention lacks support by either a specific and substantial asserted utility or a well established utility. Applicants respectfully traverse.

The Action discounts Applicants assertion regarding the identity of the molecules of the present invention and therefore, their accepted and well-established utility. "Applicants argue that utility of DNA molecules of SEQ IN NO: 1 is supported by GENBANK Accession No: AJ300837 (Exhibit C) describing a sequence that encodes a neutrolysin (*sic*; neurolysin)." Apparently the relationship between SEQ ID NO: 1 and GENBANK Accession No: AJ300837 describing neurolysin is unclear. To clarify the issue Applicants respectfully submit that the 2115 base sequence of SEQ ID NO:1 is essentially wholly contained withing the 2890 base sequence of GENBANK Accession No: AJ300837. And that the nucleic acid sequence of SEQ ID NO:1 represents the portion of GENBANK Accession No: AJ300837 that encodes functional protein. To further clarify and support this assertion Applicants respectfully submit an amino acid sequence comparison between SEQ ID NO:2 of the present invention and the amino acid sequence of GENBANK Accession No: CAC27329 (Exhibit annotated by third party scientists, wholly unaffiliated with Applicants, as encoding neurolysin (Homo sapiens). Therefore, it is clear that the amino acid sequence of the present invention is neurolysin and that the nucleic acid of SEQ ID NO:1 encodes human neurolysin.

On the last line of page 2, the Action states that "Even if the coding regions of both sequences are different only in three nucleotide positions that does not mean that the polypeptide encoded by SEQ

ID NO: 1 has the same activity as that encoded by GENBANK Accession No. AJ30083." Applicants assume that the Examiner is referring to the possibility that a change in 3 nucleic acids can alter the encoded amino acid sequence and thus potentially alter the protein's structure and effect its function. While this is true in theory, those of skill in the art who have had the misfortune to have tried to alter a proteins function by altering a single amino acid have found that most changes have no apparent effect and this is why those rare changes that do effect activity are reportable events, worthy of publication. However, the application of this issue to the present application is rendered moot by the evidence provided by the amino acid alignment of current Exhibit C, in which the amino acid sequence of the present invention is shown to be identical to that of human neurolysin (GENBANK Accession No: CAC27329). As there are clearly no amino acid differences between the protein of the present invention and human neurolysin, it is highly unlikely that they do not have the same activities and functions.

According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001). As Applicants have provided evidence that the sequences of the present application encode neurolysin and the biological significance, function and utility of neurolysin (EC3.4.24.16) are well known to those of skill in the art, in addition to the example provided in Applicants previous response (Paper No. 9), see the recent review published by Shrimpton, Smith and Lew (Endocr. Rev. 2002 Oct; 23(5):647-64 (abstract included as Exhibit D). Given this clear and convincing evidence that those skilled in the art would identify the current sequences as neurolysin (they have) and thus would recognize the well-established utility of the present invention, there can be no question that Applicants' asserted utility for the described sequences is "credible." As such, the scientific evidence of record clearly establishes that Applicants have described a utility in full compliance with the provisions of 35 U.S.C. section 101, and therefore, Applicants respectfully request withdrawal of the pending rejection.

IV. Rejection of Claims 1-3 Under 35 U.S.C. § 112, First Paragraph

The Action rejects claims 1-3 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the claimed invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully disagree.

Applicants submit that the claims have been shown to have a specific, substantial, credible and well established utility, as detailed in section III, above. Applicants therefore respectfully request that the rejection of claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

V. Rejection of Claim 2 Under 35 U.S.C. § 112, Second Paragraph

The Action rejects claim 2 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention. Claim 2 stands rejected because the phrase "highly stringent conditions" is alleged to be indefinite. While Applicants submit that the term is sufficiently definite and defined in the specification as well as in documents incorporated by reference solely in order to progress the case more rapidly toward allowance the claim has been revised to recite the specific wash conditions defined in the specification. Applicants submit that revised Claim 2 even more clearly meets the requirements of 35 U.S.C. § 112, second paragraph. Applicants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). Based on the foregoing, Applicants submit that revised Claim 2 is definite, and thus avoids rejection and therefore, respectfully request withdrawal of this rejection.

VI. New Rejection of Claim 2(a) and (b) Under 35 U.S.C. § 112, First Paragraph

The Action next rejects Claim 2 (a) and (b) under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); "*Vas-Cath*") held that an "applicant must convey with reasonable clarity to those skilled in the

art that, as of the filing date sought, he or she was in possession *of the invention.*" *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); "*Gosteli*") held:

> Although [the applicant] does not have to describe exactly the subject matter claimed, ... the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

Gosteli at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988); "*Utter*"), held "(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses" (*Utter*, at 1714). Therefore, all Applicants must do to comply with 35 U.S.C. § 112, first paragraph, is to convey the invention with reasonable clarity to the skilled artisan.

Further, the Federal Circuit has held that an adequate description of a chemical genus "requires a precise definition, such as by structure, formula, chemical name or physical properties" sufficient to distinguish the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; "*Fiers*"). *Fiers* goes on to hold that the "application satisfies the written description requirement since it sets forth the ... nucleotide sequence" (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Univ. of California v. Eli Lilly and Co.*:

> In claims to genetic material ... a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the *sequence itself.*

The Action (page 4-5)rejects Claim 2, part a)"because it does not indicate the function of the isolated nucleic acid molecule and the specification characterizes this DNA molecule by the function of encoding the polypeptide of SEQ ID NO:2 that has no specific function." The Action also rejects Claim 2 part b) due to alleged concerns that "The genus of DNA molecules selected by the hybridization process is a large variable genus".

Applicants respectfully submit that the rejection of each part of Claim 2 separately is not proper, because Claim 2 has two limitations, the first being that molecules which encode the amino acid sequence shown in SEQ ID NO: 2; and the second being hybridization under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof and covered nucleic acid molecules must meet both conditions, not just one. Applicants submit that the nucleic acid molecules identified by the intersection of both parts of Claim 2, those that encode the amino acid sequence shown in SEQ ID NO: 2; and hybridize under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof, is a finite and well defined group, which those of skill in the art could easily identify and would know how to make and use. Therefore, Applicants respectfully request that these new rejections of Claim 2 under 35 U.S.C. § 112, first paragraph, be withdrawn.

VII. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Walicka have any questions or comments,

or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

This response is timely filed and Applicants believe no fees are due in connection with this response. However, should this be incorrect the Commissioner is authorized to charge any required fees or credit any overpayment to Deposit Account No. 50-0892.

Respectfully submitted,

November 4, 2002
Date

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Exhibit A

Marked-up Version of The Pending Claims in U.S. Patent Application Ser. No. 09/833,782

1. (Amended) An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1.

2. (Twice Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO:2; and

(b) hybridizes under highly stringent conditions including washing in 0.1xSSC/0.1% SDS at 68°C to the nucleotide sequence of SEQ ID NO:1 or the complement thereof.

3. An isolated nucleic acid molecule comprising a nucleotide sequence encoding the amino acid sequence shown in SEQ ID NO:2.

4.(New) An expression vector comprising a nucleic acid sequence of Claim 3.

5.(New) A cell comprising the expression vector of Claim 5.